The Use of Auto-Titrating Continuous Positive Airway Pressure for Treatment of Adult Obstructive Sleep Apnea

An American Academy of Sleep Medicine Review

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Summary: This paper reviews the efficacy of auto-titrating continuous positive airway pressure (APAP) for treatment of obstructive sleep apnea. It is based on a review of 30 articles published in peer review journals conducted by a task force appointed by the American Academy of Sleep Medicine to develop practice parameters for use of APAP devices for treatment of obstructive sleep apnea (OSA). The data indicate that APAP can be used to treat many patients with OSA (auto-adjusting) or to identify an effective optimal fixed level of continuous positive airway pressure (CPAP) for treatment (auto-titration). Patients with significant congestive heart failure, chronic obstructive pulmonary disease (COPD), or significant amounts of central apnea were excluded from many treatment trials and there is insufficient evidence that APAP can be used to treat these patients. Many clinical trials have been performed in patients already on CPAP or with the initial APAP night in a laboratory setting. At this time only a few studies have evaluated initial titration with APAP in CPAP-naïve patients in an unattended setting. Further studies of APAP in this circumstance are needed. No studies have systematically compared the efficacy of one APAP technology with another. Devices using different technology may not give the same results in a given patient. Devices solely dependent on vibration may not work in non-snorers or patient who have undergone upper-airway surgery. High mask or mouth leaks may prevent adequate titration in devices monitoring snoring, flow, or impedance (forced oscillation technique). Review of the raw data to identify periods of high leak was performed in several of the APAP titration studies, to identify a pressure for fixed CPAP treatment or to determine if the titration was adequate. There is conflicting evidence for and against the premise that treatment with APAP increases acceptance and adherence compared to fixed CPAP. In studies demonstrating an increase in adherence with APAP, there was similar improvement in measures of daytime sleepiness as with fixed CPAP treatment. Further studies are needed to determine if APAP can increase acceptance or adherence with positive pressure treatment in patients with OSA.

Key words: Obstructive sleep apnea; CPAP; auto-titrating CPAP; autoPAP; APAP

1.0 INTRODUCTION

OBSTRUCTIVE SLEEP APNEA (OSA) IS A VERY COMMON DISORDER AFFECTING 2%-4% OF THE ADULT POPULATION.[1] Nasal continuous positive airway pressure is the most reliably effective treatment for patients with moderate to severe OSA.[2-4] This treatment has been demonstrated to reduce both subjective and objective measures of daytime sleepiness in randomized placebo controlled trials.[5,6] The conventional approach to CPAP treatment utilizes a pressure titration in the sleep laboratory during attended polysomnography. The goal is to identify an effective pressure that will prevent apnea, hypopnea, snoring, and respiratory effort-related arousals in all body positions and sleep stages. In general, higher pressures are needed in the supine position and during REM sleep.[7] Higher pressures are also needed to eliminate residual snoring and respiratory effort-related arousals (RERAs) associated with airflow limitation than to prevent apnea and hypopnea.[8,9] Attended studies allow the technologist to adjust the pressure to meet changes in body position and sleep stage and to intervene for mask leaks or persistent hypoxemia after airway patency is restored.[10] Temporary reductions in pressure may also be necessary to allow patients to return to sleep after prolonged awakenings. Attended titration is relatively expensive and time intensive; a single technologist can rarely effectively titrate more than two patients at a time. Furthermore, with the common use of partial or "split" night studies (first portion diagnostic, second portion CPAP titration), some patients will not have enough supine or REM sleep on positive pressure to allow for an estimate of the pressure requirements in all circumstances.[11,12] Thus, in some patients an optimal pressure effective in all situations cannot be identified on a single study night. In addition, the optimal pressure may well be higher than necessary for much of the night as the needed CPAP pressure can vary considerably with sleeping posture and sleep stage.[7] For example, a pressure of 16 cm H_2O may be needed for supine REM sleep while a pressure of 10 cm H_2O may work well during NREM sleep in the lateral sleeping position.[7] The use of a single higher pressure for the entire night could potentially increase mask leaks, mouth leaks, pressure intolerance, and theoretically reduce acceptance and adherence with CPAP treatment in some patients. A major challenge facing clinicians treating OSA is increasing CPAP acceptance and adherence.[13-15] The optimal pressure could also change with time, secondary to multiple factors including weight gain and nasal congestion. When OSA patients on treatment with nasal CPAP complain of persistent sleepiness despite adequate adherence, a re-titration study may be deemed necessary to ensure a correct pressure setting. Finally, some OSA patients simply do not have ready access to a sleep laboratory because of their location. In addition, some sleep centers have considerable scheduling backlogs that delay access to timely care.

Accepted for publication December 2001
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Because of these problems with the traditional approach to CPAP treatment and titration, auto-titrating devices (APAP) have been developed. Today, a wide variety of APAP units are available.[16-21] They vary in which physiological variables they monitor (snoring, apnea, hypopnea, airflow limitation, impedance, or a combination of variables) and in their algorithms to respond to these factors. APAP devices are designed to increase pressure as needed to maintain airway patency and then to decrease pressure if no events are detected over a set period of time. Because the minimum effective pressure is delivered (auto-adjusting), the mean pressure is often lower than the optimal fixed CPAP pressure. It has been hypothesized that this lower pressure could increase acceptance and adherence with chronic positive pressure treatment.[17,18] Most APAP units have the ability to store pressure versus time data and many can also record leak, apnea, and hypopnea information. This information can be transferred to a computer and analyzed quickly to provide both summary information and more detailed pressure and leak versus time plots on selected nights. One could then choose either the maximum pressure or a pressure thought satisfactory for the majority of the time as the optimal effective CPAP level for chronic treatment (P_{eff}). Those units storing apnea and hypopnea information can also be used for diagnosis when the machine is set at a low fixed pressure. APAP devices generally cost more than fixed CPAP devices. This, in part, has limited their widespread use for chronic treatment. Cost is less of a factor if the devices are to be used for auto-titration to determine a fixed CPAP level. A few units then could be used to perform many unattended CPAP titrations. However to realize cost savings, APAP devices would need to reliably perform adequate unattended pressure titrations on a majority of CPAP-naïve patients. The cost savings of this approach has not been proven.

In summary, there are several potential uses for APAP devices. These include: 1) laboratory or unattended determination of an appropriate CPAP level to provide the prescription pressure for fixed CPAP (FCPAP) treatment, 2) as a chronic treatment of OSA, using varying pressures during the night which might increase acceptance and adherence, and 3) screening devices for identification of OSA. In this review only the evidence for efficacy of APAP in the first two potential uses will be analyzed.

2.0 PURPOSE

A task force was appointed by the Standards of Practice Committee (SPC) of the American Academy of Sleep Medicine (AASM) and assigned the task of developing a critical review of the literature pertaining to the treatment aspects of APAP devices. This review provided the basis for the development of practice parameters by the SPC. All members of the task force completed conflict of interest documents and were found to have no significant conflicts relevant to this subject. The Board of Directors of the American Academy of Sleep Medicine approved this review.

3.0 METHODS

A literature search (Medline and EMBASE 1980-June 2001) for articles on treatment with auto-titrating CPAP (APAP) was conducted. Key words for searches included autoCPAP, automatic CPAP, auto-titrating CPAP, self-titrating CPAP, self CPAP, autoset, auto PAP, and auto-adjusting CPAP. Each search was run separately and findings were then merged. When the search was limited to articles published in English, a total of 55 articles were identified. The set of articles was further reduced to include only those with a major focus on treatment that were published in peer reviewed journals. Studies with a major focus on treatment were defined as: 1) those determining APAP efficacy either as chronic treatment or as a means for determining an optimum pressure for fixed CPAP treatment, or 2) those determining the effect of APAP on positive pressure acceptance and or adherence. Several reviews, editorials, and articles appearing in journal supplements were included in the references;[16-22] however these were not used to form conclusions. Thirty articles[23-52] were selected for inclusion in the evidence tables. Because there was relatively little evaluation of safety and side effects of APAP in patients with central apnea or cardiopulmonary disease, one case report was included,[26] and one study of an auto-titration device designed entirely for selection of a fixed pressure (by post-study physician review) for chronic treatment were included.[34]

Two task force members analyzed each article for design, inclusion and exclusion criteria, outcome measures, biases, and conclusions. The level of evidence of each article is listed according to criteria as noted in the accompanying Standard of Practice parameter paper. For purposes of determining if a study meets historical standards,[53] an AHI of < 10/hour of sleep on CPAP or APAP was considered an acceptable outcome for positive pressure titration in OSA patients.

4.0 BACKGROUND

4.1 Technology

There have been several articles reviewing clinical experience with APAP devices.[6-18] Published editorials have also discussed the potential uses and limitations of the machines.[19-22] A number of different auto-titrating CPAP devices are commercially available. They vary with respect to what physiological variable is monitored to decide changes in pressure and the algorithms (decision paths) used to determine if and how much to increase or decrease pressure. In general, the devices measure some or all of the following: snoring (airway vibration), airflow (apnea or hypopnea), and the flow vs. time profile (evidence of flattening as a surrogate for airflow limitation). Devices using the forced oscillation technique to monitor impedance have also been developed.[38,39] In order to detect changes in airflow, some units utilize a built-in pneumotachograph to quantify flow and the flow versus time profile, while other machines use differences in blower speed during inspiration and exhalation. Actual tracings illustrating the changes in pressure in response to different respiratory variables can be found in the references for airflow,[31] airway vibration,[38] inspiratory airflow flattening,[17,50] and impedance.[42]

Most APAP devices start with a baseline pressure (usually around 3-4 cm H_2O) and then titrate upward as needed. An absence of monitored events then prompts a gradual decrease in pressure. This allows the minimum effective pressure to be delivered in a given circumstance. The APAP devices usually allow the clinician to set maximum and minimum pressure limits. The machines usually start at a low pressure (which can be specified in some) and after some brief initial period the pressure rises until the low pressure limit is reached. From this point, auto-titration begins. The Morphee-plus device[39,46] is unique in that the clini-

cian must supply a reference pressure (P_{ref}). The machine then titrates within a range about this pressure (For example, P_{ref} – 4 cm H_2O, P_{ref} + 2 cm H_2O). The P_{ref} can be determined by a previous conventional CPAP titration or estimated by a formula.[39,46]

The problems of how to handle mask/mouth leak and central apnea have provided a challenge for the designers of APAP. However, these two problems are not unfamiliar to technologists performing attended CPAP titration. Mask/mouth leaks tend to raise the baseline flow delivered by units and diminish the variations in flow during inspiration and expiration. The resulting airflow signal may be interpreted as an apnea or hypopnea and prompt an increase in pressure that may further increase leak. In impedance-based systems, a mask leak results in a spurious low impedance that does not reflect the actual state of the airway.[21] Teschler and Berthon-Jones reported on their clinical experience in 1000 patients using the Autoset T APAP device[18] and estimated that leak exceeded 0.4L/s on average for 10% of a supervised night and 15% on an unsupervised night. To handle the leak problem many units have algorithms that limit pressure increases when leak exceeds certain values or when increases in blower speed no longer result in increases in mask pressure. Other units have leak alarms that could prompt the patient/staff to readjust the mask. Mouth leaks could be approached by treating nasal congestion, using heated humidification, chin straps, or using a mask covering the nose and mouth.

Central apnea during APAP treatment/titration is another difficult problem in some patients. Central apneas of the Cheyne-Stokes type are common in patients with severe congestive heart failure (CHF)[54] and also can occur in patients with neurological diseases. Central apneas may appear in patients with OSA and CHF during a CPAP titration after the airway obstruction is reversed.[55] Other patients with OSA may have central apneas after arousals[56] that are sometimes prompted by excessive pressure. While CPAP has been reported to decrease the AHI in both idiopathic central apnea,[57] and central apnea associated with congestive heart failure,[58] in many patients, increases in pressure will not decrease events or may increase the problem. Some device manufacturers have attempted to identify central apnea by detecting cardiac oscillations in the airflow tracing (open airway apnea). However, the airway can close in central apnea.[59] Others have designed algorithms that limit the pressure increases for apnea in the absence of associated snoring or airflow limitation. However, the problem persists in some patients and many of the reviewed clinical trials excluded patients with congestive heart failure.

4.2 Use of APAP for CPAP Titration

Auto-titrating devices can be used to determine an optimal fixed level of CPAP for long term treatment with a conventional CPAP device. This could be performed as an attended study (which allows technologist intervention) or as an unattended study either in the sleep laboratory or at home. In the sleep laboratory APAP units could potentially allow a given technologist to titrate more patients (technologist extender). Interventions for mask leaks and the treatment of persistent hypoxemia despite a patent airway with supplemental oxygen would be possible. However, performing unattended CPAP titration in the sleep laboratory or home is potentially the most useful application of APAP devices. Patients without rapid access to a sleep laboratory, either because of their location or a long wait for the next available appointment, could be titrated and started on treatment. There is also a potential for cost savings but this would depend on whether the diagnostic study was performed in a traditional sleep laboratory or as an ambulatory study.[19,31] For example, the cost of an in-laboratory diagnostic sleep study, plus unattended APAP titration might not differ that much from the cost of one in-laboratory split night study. The potential for cost savings would also depend on whether or not APAP could reliably perform adequate titrations in CPAP-naïve patients. The need to repeat a significant number of CPAP titrations in the sleep laboratory could negate any potential cost savings. Fletcher and coworkers did find a considerable estimated cost savings with a protocol using both home diagnostic monitoring and auto-titration.[31] However, the assumption that unattended APAP titration would result in overall cost savings is not yet confirmed by published data from randomized trials.

To be effective, unattended titration would require that the patient be well educated about using the device and able to apply the mask properly and adjust it if leaks occur.[18] Proper mask fitting would also be essential. Furthermore, as discussed below, judicious patient selection for unattended APAP titration, knowledgeable physician review of stored information for the APAP device, and timely follow-up of the outcome of CPAP treatment using an APAP selected pressure would appear to be needed to ensure a good clinical outcome.

APAP devices allow transfer of pressure over time information to a computer for analysis. Some reveal only the percentage of time at each pressure while others record more detailed information such as leak and persistent apnea/hypopnea counts. Given sufficient and reliable data, the clinician could then review the data and decide on an appropriate fixed pressure. Two common alternatives are to identify either the maximum pressure or a pressure only rarely exceeded (95th percentile pressure). The 95th percentile pressure (P_{95}) is the level of pressure exceeded only 5% of the time. Most devices will display a plot of the percentage of time each pressure is applied and will compute pressure statistics (P_{mean}, P_{95}, and $P_{maximum}$) over a selected number of days. The ability to store more than one night of data is useful, as more than one night may be needed to effectively select an appropriate fixed pressure. However, longer periods of titration may potentially increase cost. In most published studies, investigators viewed some form of raw data to eliminate periods of high mask leak or determine if the titration was technically adequate. Many devices respond to high leak with increases in pressure often up to a set maximum pressure.

4.3 Chronic Treatment of OSA with APAP

The second potential use for APAP devices is for chronic treatment of OSA. However, an advantage in acceptance, adherence, or other outcomes with APAP compared to fixed CPAP would need to be demonstrated to justify the routine use of APAP units. It has been proposed that by allowing treatment with the lowest effective pressure that acceptance or adherence will be enhanced. In contrast to APAP, a treatment pressure for fixed CPAP must be chosen to provide a pressure effective in all body positions and sleep stages. In some patients this pressure may be much more than is needed for some of the night. For example, a patient requiring 16 cm H_2O in the supine position during REM sleep

may only need 10 cm H_2O in the lateral sleeping position during NREM sleep. The mean pressure in such patient would be lower on APAP if a significant amount of sleep time is spent in the lateral position. How much lower the mean delivered APAP pressure would be than a fixed CPAP pressure depends on the relative time spent in the supine and non-supine positions and as well as the amounts of NREM and REM sleep. The difference in pressures needed in those situations also determines the potential for differences in mean pressure between APAP and CPAP treatment. For example, if 14 cm H_2O pressure was needed in the lateral sleeping position and 16 cm H_2O in the supine position there would be relatively little potential for lowering of mean pressure with APAP. In some studies, the difference in mean APAP pressure and fixed CPAP pressure was on the order of 1-2 cm H_2O but can be greater with some APAP devices and groups of patients. The difference between the fixed optimal CPAP level and the mean pressure on APAP can vary considerably between patients.[44]

Contrary to the idea that APAP could improve acceptance and/or adherence, many patients do not find pressure intolerance to be their major discomfort with CPAP treatment. Other factors contributing to dissatisfaction with CPAP besides pressure intolerance may potentially limit the ability of APAP to increase acceptance and/or adherence. In one study the nasal mask interface was the major reason of discontinuing treatment.[13] Nasal congestion and dryness are also major side effects. Studies have shown that education, close support during treatment initiation, the addition of humidification, and close follow-up can improve acceptance and adherence.[14,15]

5.0 QUESTIONS TO BE ADDRESSED

The 30 articles[23-47] listed in Table 1 were used to try to answer several important questions about the evidence for clinical effectiveness of APAP. There were several factors complicating the analysis. First, there are many different devices and findings from one device may not extrapolate to others. Second, many of the studies were clinical series in which use of the device was shown to be clinically feasible and effective but not compared to conventional CPAP treatment or placebo. The entry criteria were not always clearly stated so that in some studies there may have been a selection bias. Third, even when randomized controlled trials were performed, the designs varied significantly. Included in Table 1 is a brief outline of each study design.

5.1 What is the evidence that APAP can effectively reduce the AHI in OSA patients?

A total of nine clinical series,[23,27,31,32,37,38,41,42,52] one non–randomized control trial[27] and 16 randomized controlled trials[24,28-30,35,37,39,40,43-46,48,50-52] found that APAP reduced the apnea plus hypopnea index to acceptable levels (AHI <10/hr) in greater than 80%-95% of the OSA patients studied. Of note, the randomized controlled trials were designed to answer other questions (such as comparing fixed CPAP and APAP). That is, there was no placebo treatment and the diagnostic study always preceded the APAP study.

As stated previously, many studies excluded patients with congestive heart failure or chronic lung disease. None of the above studies included patients with a substantial amount of central apnea at baseline. Most patients had already had a formal sleep study and some had a traditional CPAP titration before being exposed to APAP for the first time. In some studies that patients undergoing a night of APAP were already being treated with CPAP. The results in such patients may differ from naïve, untreated patients.

The devices studied included those using snoring alone;[23,24,38,40,48] apnea and hypopnea;[39,46] apnea, hypopnea, and snoring;[27-29,31,45] snoring, apnea, hypopnea, and flow limitation;[32,50-52] and the forced oscillation technique.[30,41-44]

In several studies there were reports of a few patients in whom the titration was inadequate. Lofaso and coworkers[38] using a snoring-based device reported that 3 of 15 subjects had an apnea plus hypopnea index (AHI) >10/hr. These included one non-snorer and two mouth breathers. Teschler et al.[50] reported that one of 21 patients had such a severe mask leak that auto-titration was not possible. In this patient the pressure increased to the preset maximum pressure of 20 cm H_2O. In another four subjects there were transient inappropriate pressure increases during periods of large leaks requiring reseating of the mask. The APAP device used in this study monitored snoring, airflow (apnea and hypopnea), and airflow flattening.

While the above discussion utilizes a reduction in the AHI to less than 10/hr as the criterion for acceptable treatment,[53] reductions to less than 5/hr and elimination of significant airflow limitation as well as apnea/hypopnea may be required for reversal of sleepiness in individual patients.[8,9,60] In some studies, the mean AHI was in fact reduced to less than 5/hr[27,29,30,35,41-43,45,47,50,52] on APAP. While patients with the upper-airway resistance syndrome (UARS) were included in some studies,[33] no study specifically evaluated the effectiveness of APAP in patients with UARS or very mild OSA (AHI 5-15 events/hour).

5.2 What is the evidence that APAP can reduce the AHI as well as conventional CPAP either in a laboratory titration or as chronic treatment? Is the mean pressure lower on APAP devices?

The literature search identified two clinical series,[41,42] one non-randomized control trial,[27] and 11 randomized control trials[24,28-30,35,39,43,44,46,48,52] that compared the AHI on a night on APAP with a night of fixed CPAP where the pressure level (P_{eff}) was determined during a previous conventional CPAP titration. An additional two studies[50,51] compared a night of manual CPAP titration to an attended APAP titration (random order) and also to a night of fixed CPAP at an optimal pressure determined as P_{95} on the APAP night (order not random). Comparisons between APAP and fixed CPAP (FCPAP) could be influenced by the type of APAP machine as well as the criteria and airflow measurement technology used for CPAP titrations. For example, monitoring airflow with a pneumotachograph is likely to detect more events than with a thermistor. The mean AHI in all studies was very similar on APAP and fixed CPAP nights (Table 1). Thus, therapy with APAP and fixed CPAP (P_{eff} by manual titration or auto-titration) appear to give similar treatment night AHIs.

If reduction in the AHI is similar with APAP and CPAP, does APAP treatment result in a lower mean or median treatment pressure? Considering investigations comparing APAP and CPAP (P_{eff} determined by conventional titration), there were nine stud-

ies in which the APAP mean or median pressure was lower[24,27,30,41-44, 48,50] and one[29] in which the mean treatment pressure was slightly higher. In the latter study, APAP was constrained to vary within a fairly tight range (6 cm H_2O). In the studies showing a decreased mean or median pressure on treatment nights, the difference was usually 6 cm H_2O or less and often 1-2 cm H_2O.

Differences between the fixed CPAP and mean APAP pressures were 3.1,[24] 2.6,[27] 0.9,[28] and 2.2 cm H_2O.[48] Another study found the median APAP pressure to be 1.8 cm H_2O lower.[52] Randerath et al.[44] presented a detailed distribution of the difference between fixed and mean APAP pressures by the forced oscillation technique in a group of 52 patients. The fixed pressures exceed the mean APAP by as much as 6 cm H_2O although in 34 patients the difference was between 1 and 4 cm H_2O.

5.3 What is the evidence that APAP can effectively improve sleep quality and subjective and objective measures of daytime sleepiness in OSA patients?

When APAP was first introduced there was concern that frequent pressure changes might trigger arousal. Frequent arousals could reduce the potential benefit from treatment even if the AHI were significantly reduced. However, most APAP algorithms utilize a fairly slow increase (or decrease) in pressure depending on the events detected. For example, an increase of 1 cm H_2O over several minutes occurs if snoring is detected. In routine manual pressure titration, increments in pressure are rarely less than 1 cm H_2O and are typically more sudden than changes with APAP. Thus, one might suppose that with the proper algorithms, arousals would not necessarily be more frequent with APAP than conventional CPAP titrations.

In general, the literature documents that APAP significantly improves sleep quality. If one defines improved sleep quality as a treatment arousal index of less than or equal to 20 events per hour or an increase in either slow wave or REM sleep (or both) compared to baseline, then a number of studies document improved sleep on APAP. A total of four clinical series,[37,38,41,52] one non-randomized control trial[27] and 11 randomized controlled trials[24,28-30,35,39,43-45,48,50] found some evidence that APAP improved sleep quality. Two of the studies listed as clinical series[37,52] were actually randomized controlled studies with respect to different outcome measures than improvement in sleep quality.

In the clinical series there was variability in which sleep quality variables improved. Lloberes et al.[37] compared sleep quality in a group of OSA patients undergoing partially attended APAP titration with a smaller group of OSA patients with an equivalent AHI who had previously undergone conventional titration (not a true randomized controlled comparison). The groups had a similar sleep quality on the positive pressure titration nights (APAP titration: arousal index 12±7/hr, conventional CPAP titration: arousal index 11±6/hr). Lofaso and coworkers[38] found an increase in slow-wave (71±86 vs. 102±149 minutes) but not REM sleep on APAP compared to baseline. Randerath et al.[41] found an increase in REM sleep (diagnostic: 42.7±16.4, APAP mode 1: 66.6±23.4, and APAP mode 2: 61.1±24.6 minutes) but no change in slow-wave sleep using the forced oscillation technique for APAP. There was also a decrease in the respiratory arousals/hour (diagnostic: 20.9±16.6, APAP mode 1: 2.3±3.7/hr, and APAP mode 2: 4.5±5.2, $p<0.001$). Alternatively, in a latter study, the same group using a similar technique, found a decrease in total sleep time (340.0±55.9 minutes at baseline, 287.8±47 on APAP mode 1, and 287.8±49.5 on APAP mode 2, $p<0.05$) and no change from baseline (diagnostic study) in the arousal index in a group of patients with mild OSA.[42] In a subsequent investigation by the same group, using APAP with forced oscillation technique, sleep quality (increased REM sleep, decreased arousal index) improved on APAP compared to baseline.[43] The amount of REM sleep increased from 47.4±25.3 to 63.4±27.2 minutes ($p<0.05$) and the respiratory arousal index decreased from 17.8±15.8 to 3.3±3.9 events/hr ($p<0.001$). Teschler et al.[52] found an increase in slow-wave sleep from 10.2±2.2 to 24.6±2.8 as a % of total sleep time ($p<0.01$) and an increase in REM sleep from 11.7±2.3 to 25.9±1.4% total sleep time ($p<0.001$) on APAP nights compared to the diagnostic night. There was also a decrease in respiratory arousals from 42±7.2/hr to 4.8±0.8/hr ($p<0.001$). Boudewyns et al.[27] found that APAP increased the mean amount of REM sleep (26.0 to 101.5 minutes, $p<0.05$) and decreased the mean arousal index (27.4 to 8.4 events/hour, $p<0.05$) compared to baseline (no treatment).

One might also ask if APAP was as effective as conventional CPAP for improving sleep quality. In general, the literature support the idea that the improvement in sleep quality with APAP and conventional CPAP is similar. In seven randomized controlled trials[24,28-30,43,46,48] APAP and fixed CPAP resulted in equivalent sleep quality (reduction in arousal index, increased slow wave and REM sleep). Behbehani and coworkers[24] found a significant increase in slow-wave and REM sleep on APAP compared to the diagnostic night. The number of sleep stage shifts was also significantly decreased on CPAP (180.2±53.8) and APAP (174.5±55.3) compared to the diagnostic night (227.4±73.7 shifts, $p<0.05$). The increases in slow wave sleep and REM and the decreases in sleep stage shifts were not significantly different between CPAP and APAP. D'Ortho et al.[28] found the minutes of stage 3 and 4 sleep not to differ on CPAP (94±40) and APAP night (87±40) but to be significantly different from baseline (44±36) on both treatments. In a similar manner there was a similar decrease in awakenings and arousals per hour on CPAP (13.7±8.0/hr) and APAP (15.5±8.9/hr) compared to baseline (45.6±25.8/hr) ($p<0.05$). The amount of REM as a %TST also increased on CPAP (22±5) and APAP (21±8) compared to baseline (16±5%). Ficker and coworkers[29] found an equivalent arousal index on fixed CPAP (7.0±4.3) and APAP nights (7.4±4.1/hr). The same group using a different APAP device[30] found an increase in slow-wave and REM sleep compared to baseline on both CPAP and APAP nights. The amounts of slow-wave (APAP: 19.3±6.6 and CPAP: 18.4±7.2 % total sleep time) and REM sleep (APAP: 21.7±4.9 and CPAP: 19.8±6.8% total sleep time) were very similar. Randerath and coworkers[43] found the amount of REM sleep (% total sleep time) to increase compared to baseline on the first night of APAP or CPAP with equivalent amounts of REM on APAP (19±6%) and CPAP (19±6%) nights. The respiratory arousals also decreased compared to baseline (24±23.2 events/hour) vs. APAP (1.8±3.7) and CPAP (1.9±2.9) nights. Sharma and colleagues[48] using a crossover design found that both fixed CPAP and APAP increased the amount of slow-wave sleep and REM sleep compared to baseline. However, the amount of slow-wave sleep (as % of total

sleep time) did not differ on CPAP (16.7±9.8%) and APAP (17.1±9.3%) nights. Similarly the amounts of REM sleep (as a % of total sleep time) on CPAP (22.7±7.9%) and APAP (25.3±7.4%) nights did not differ. Using a parallel group design, Sériès et al. compared fixed CPAP with two modes of APAP.[46] The amount of stage 3 and 4 increased and the arousal index decreased in all three groups. There was no difference in the improvements with CPAP and the two modes of APAP.

Two randomized controlled studies[35,45] found that APAP improved slow-wave sleep more than conventional CPAP. Konermann et al.[35] found that slow-wave sleep (% total sleep time) increased from 11.4±10.4% on a diagnostic night to 17.6±18.4% on CPAP vs. 13.2±12.2% to 27.2±16.5 on APAP using a parallel group study design. The improvement on APAP was significantly greater than on CPAP ($p<0.01$). Scharf and coworkers[45] recorded 16.1±22.7 minutes of slow-wave sleep on conventional CPAP and 32.6±27.4 minutes on APAP, $p<0.05$ using a crossover design. In another study where snoring elimination was a goal of the APAP, but not the conventional CPAP, titration found that APAP resulted in a slightly but significantly lower arousal index.[50] However this difference is most likely the result of different titration goals.

If APAP is used to select a fixed pressure for fixed CPAP treatment, does treatment using this pressure result in equivalent improvements in sleep quality? Berkani et al.[25] determined the optimum CPAP pressure using APAP. On a subsequent night patients slept on CPAP at this pressure and sleep quality was compared to the diagnostic study. Slow-wave sleep increased from 18±26 to 73±21 minutes on CPAP and REM sleep increased from 36±29 min to 69±32 min (both $p<0.05$). In addition the arousal index decreased from 47±14 to 8.3±3 on CPAP ($p<0.05$). Gagnadoux and coworkers[32] also used APAP to select a fixed pressure for CPAP treatment. After two months of CPAP, a study on this treatment was preformed. Slow-wave sleep (% total sleep time) increased from 17.4 to 39.5% ($p<0.001$) and REM sleep increased from 9 to 18.8% ($p<0.001$) compared to the diagnostic night.

Another method of assessing the effectiveness of APAP is to determine if subjective (Epworth sleepiness scale = ESS) or objective measures of daytime sleepiness improved after APAP treatment. D'Ortho et al.[28] using a randomized crossover design found the ESS to improve after CPAP (9.2±5.5) and APAP (9.3±4.8). The ESS values after both treatments were significantly lower (less sleepiness) than at baseline (12.7±5.3) ($p<0.05$). However, the ESS after CPAP and APAP were not significantly different from each other. Ficker et al.[29] found similar ESS after APAP (5.3±3.9) and CPAP (6.5±4.3) treatments using a randomized crossover design. The same group in a later study[30] found the ESS after APAP and CPAP to both be significantly lower than baseline (13.3±3.0). However, the ESS values after APAP (5.6±1.8) and CPAP (5.3±1.6) were essentially the same. Fletcher et al.[31] used a protocol with ambulatory diagnostic monitoring followed by unattended APAP titration with ambulatory monitoring to determine if adequate treatment on APAP was possible. Those having adequate APAP titrations had repeat Epworth sleepiness scale and MSLT testing after a minimum of three weeks of APAP treatment. After therapy the ESS was significantly lower (10.5±0.9 vs. 16.8±0.6, $p<0.01$) and the nap sleep latency was significantly greater than at baseline (5.7±0.81 vs. 3.7±0.6, $p<0.01$). Meurice and coworkers,[39] using a parallel group design, found similar and significant decreases in the ESS compared to baseline on APAP (15.2±4.2 reduced to 5.6±3.7) and fixed CPAP (14.4±6.3 reduced to 8.6±6.9). The amount of reduction in the ESS did not differ between APAP and fixed CPAP. In this study, increases in the maintenance of wakefulness test (less sleepiness) compared to baseline were also similar between APAP and fixed CPAP. The MWT latency increased from 18.2±11.2 minutes to 26.9±12.0 minutes on APAP and from19.0±13.9 to 26.1±14.6 minutes on CPAP. Again, the improvements were not statistically different between APAP and CPAP. Hudgel and Fung,[33] using a randomized crossover comparison of APAP vs. CPAP, found that the baseline ESS was reduced from 16±0.8 to 8±1 post-CPAP and 9±1 post APAP (p=NS, APAP vs. CPAP). Sériès et al.[46] found that CPAP and two modes of APAP treatment each resulted in equivalent falls in the ESS and increases in sleep latency on the maintenance of wakefulness test compared to baseline using a parallel group design.

There is also evidence that a fixed CPAP pressure determined by APAP titration can result in a good outcome. Gagnadoux et al.[32] found a significant reduction in the ESS (11.4±5.4 to 5±4, $p<0.05$) after treatment with CPAP using a pressure determined by a previous APAP titration. Sériès and coworkers[47] also studied the effects of CPAP with an effective pressure chosen by APAP titration (unattended). After CPAP treatment the Epworth sleepiness scale was reduced significantly from 15±4 to 7±3. Stradling and coworkers[49] used a parallel group design to compare outcomes of fixed CPAP treatment chosen either by conventional or APAP titration. For those patients accepting therapy, the ESS reduction was similar at six weeks with manual titration (from 14.4±4.6 to 7.3±3.0) and APAP titration (from 14.7±5.2 to 8.9±4.4).

In contrast to the above documented improvements in the ESS on APAP or CPAP at a level chosen by an APAP titration, Boudewyns et al.[27] found no improvement in the ESS after one month of APAP treatment. The ESS at baseline was 4.0 (confidence interval (CI) 2 to 7) and after APAP was 6.0 (CI 4 to 7). However, the baseline ESS was already in the normal range.

In summary, the data from the above studies suggests that APAP treatment or CPAP treatment at a pressure level determined by APAP, results in similar improvement as CPAP chosen by conventional titration, with respect to sleep quality (increases in slow wave and REM sleep and decreases in respiratory arousals). Furthermore, similar improvement is also seen in subjective and objective measures of daytime sleepiness in the OSA patients that were studied.

5.4 What is the evidence that APAP can prevent significant nocturnal oxygen desaturation in patients with OSA?

If APAP were able to adequately reduce the AHI, it is possible that significant arterial oxygen desaturation could still occur. For example, with the onset of REM sleep, it might take several minutes for pressure to increase to a level adequate to maintain airway patency with APAP. During this period, significant drops in oxyhemoglobin saturation might occur. It is possible that a technician noting significant desaturation might increase the level of CPAP more quickly. Arterial oxygen desaturation can also occur even with intact airflow. Shortly after nasal CPAP was introduced, Krieger et al.[10] reported on a patient who developed a prolonged period of hypoventilation and severe hypoxemia during

REM sleep while on positive pressure. Many sleep physicians have encountered patients with intact airflow on CPAP who have persistent oxyhemoglobin desaturation during REM sleep, presumably secondary to hypoventilation. Some of these patients with this problem will respond to additional CPAP pressure or a switch to bi-level pressure. Others may need the addition of supplemental oxygen. Because of these concerns it is relevant to assess the performance of APAP with respect to arterial oxygen saturation, particularly if these devices are to be used for unattended titration.

The studies that were reviewed used many different indices of arterial oxygen saturation. Some did not present any data about arterial oxygen saturation.[24,25,29,33,51] The patient populations did not include patients with known daytime hypoventilation or significant chronic lung disease. Therefore, the results to follow may not be applicable to those populations of patients. D'Ortho et al. found the minutes with an SaO_2 less than 90% to be 8.8±20.5 minutes on APAP and 3.6±10.3 minutes on conventional CPAP in a group using a crossover design.[28] While the means were not significantly different, the large standard deviation suggests that a few patients on APAP may have had clinically significant arterial oxygen desaturation. However, this data is not presented. Ficker et al. found no difference in the oxygen desaturation index on APAP 8.8±9.8 vs. CPAP 11.2±12.6.[30] Gangadoux and coworkers[32] found that only 0.2% of the total sleep time on APAP was at a SaO_2 less than 90%. Konnerman et al.[35] found CPAP and APAP not to differ with respect to the percentage of time above a SaO_2 of 90% (97.2% with CPAP and 99.0% with APAP). Lofaso and colleagues[38] found a mean of[39] minutes with a SaO_2<90% on APAP treatment. Meurice and coworkers 39 found the mean sleeping SaO_2 not to differ between APAP and CPAP, but no data were given with respect to the number of drops in the SaO_2 or the time below a given SaO_2 level. Miyasaki et al. used single night studies with randomized periods of conventional CPAP and APAP.[40] They found a significantly lower minimum SaO_2 on APAP (89.0±2.7%) vs. on fixed CPAP (92.8±2.5%), ($p<0.05$). However, the relative amounts of REM and supine sleep on APAP and fixed CPAP were not reported. The APAP device they used reduced the pressure by 1 cm H_2O over five minutes when no events indicating airway instability were noted. During this reduction in pressure, the investigators noted the onset of some sleep-disordered breathing events. In a study by Randerath et al.,[44] the minimum SaO_2 was 87.0±4.2 on APAP nights and 87.9±4.5 on CPAP nights (p=NS). In the study by Scharf and coworkers[45] there was no significant difference between fixed CPAP and APAP with respect to the number of 3% desaturations. Sharma et al.[48] did find a lower minimum SaO_2 on APAP than fixed CPAP (79.9±9.7% vs. 84.4±4.3%). Alternatively, when comparing APAP and traditional CPAP titration nights, Teschler et al.[50] found a significantly higher mean nadir in the SaO_2 on APAP than conventional titration nights (90.4±0.8% vs. 84.8±1.4%).

In summary, evidence to date suggests that APAP prevents significant desaturation in most OSA patients. There may be a tendency for a lower minimum SaO_2 on APAP than on fixed CPAP. However, arterial oxygen desaturation may also occur in some patients treated with fixed CPAP. The lack of arterial oxygen desaturation on a given night in the sleep laboratory with a conventional CPAP titration does not ensure that some desaturations will not occur on the fixed optimal CPAP pressure at home. For example, in some subjects an adequate amount of supine REM sleep does not occur during the initial CPAP titration. Thus, adequacy of prevention of desaturation on the highest pressure used may not be determined with certainty in such cases.

Should oximetry be performed during unattended auto-titration? This might detect those cases with significant desaturation on APAP. The above studies do not document a definite need for oximetry in most cases. However, as noted above, the patients with a high likelihood of persistent desaturation on CPAP were not studied. The need for oximetry during unattended auto-titration should be the subject of more study. Based on the current evidence, correction of arterial oxygen desaturation during APAP titration cannot be assumed without documentation with concurrent oximetry.

5.5 Are all the APAP technologies equally effective?

The literature search did not identify an article in a peer review journal that compared two APAP technologies. Thus, there is no clear evidence that one APAP technology is superior to another. However, the results from a study of one device cannot necessarily be assumed to generalize to all APAP devices. Some have suggested that monitoring of more than one variable may improve the results of APAP titration.[21] However, evidence is lacking to prove this hypothesis. Besides outcomes, one would expect that patients might find breathing on one device more or less comfortable than another. Considerations, such as noise, might also affect patient satisfaction. No data on the variables affecting patient satisfaction (noise, comfort) with APAP have been published. In addition, patient satisfaction studies comparing different APAP technology/devices have also not been published to date.

Two studies found that APAP devices using vibration alone may fail to work in patients with prior upper airway surgery or persons with minimal snoring.[25,32] Berkani[25] reported on 10 patients in whom P_{eff} was chosen by an APAP machine using only snoring to detect events. When these patients were studied using fixed CPAP at P_{eff}, two of the ten had an AHI >10/hr. One of these patients had a previous laryngectomy and the other a UPPP. Lofaso and coworkers[38] using a device monitoring snoring found 3 of 15 patients with an AHI >10 during an APAP treatment night. One of the patients was a non-snorer and two were mouth breathers. Of note, these studies did not address whether other technologies would have resulted in an AHI <10/hr in these patients. Miyazaki and coworkers found that a device utilizing vibration alone failed to completely normalize maximum esophageal pressure deflections.[40] However, a comparison of mean esophageal pressure deflections was not performed. Devices that use vibration may also require utilization of limited types of masks, tubing, or humidifiers as per manufacturer specifications.

APAP units monitoring flow or impedance may fail to titrate properly because of high mask leaks. Using flow alone may not result in recognition of respiratory effort related arousals. Lafond and Sériès found that two flow-based systems failed to adequately respond to increases in nasal resistance induced by histamine.[36] One device used changes in compressor speed to monitor flow and the other used a built in pneumotachograph. The authors hypothesized that a device also monitoring flow limita-

tion might have detected such a change. It is possible that devices detecting airflow flattening might titrate to a higher pressure level than those only detecting apnea or hypopnea. The difference in pressure would likely be of the order of 1-2 cm H_2O.[8] While this might result in a lower AHI, there is the potential to increase pressure intolerance. This could potentially be most important if APAP is used to select a pressure for fixed CPAP treatment. However, there was no data to suggest that eliminating airflow limitation was better or worse than other technologies. The need to eliminate airflow limitation or completely normalize esophageal pressure deflections in conventional CPAP titration is controversial.[60] Potential improvement in sleep quality with elimination of flow limitation is balanced by the potential for pressure intolerance or higher mask leaks with the higher pressure.

5.6 Is APAP effective in determining an optimal fixed CPAP pressure for chronic fixed CPAP treatment during an attended or unattended APAP titration? Does use of APAP titration affect acceptance or adherence?

To answer the first question, one can compare fixed CPAP treatment pressures selected by APAP and conventional CPAP titration or determine the outcome of fixed CPAP treatment at a pressure chosen by an APAP titration. In evaluating these studies, however, comparison of means does not tell the entire story. While means could be similar, there could be a significant proportion of patients with substantial differences in P_{eff} selected by conventional CPAP titration or APAP. There are at least two standards by which to judge APAP selection of a fixed CPAP pressure. The first is whether APAP titration will allow selection of a P_{eff} resulting in acceptable treatment (AHI<10/hr) and/or good clinical outcome. Several of the studies that were reviewed used this approach.[25,32] The second is whether APAP titration is as good as the "gold standard" (manual titration). The results of any comparison between APAP and manual titration depend on the APAP device, the method used to select the P_{eff} from the APAP titration, and the manual titration algorithm.

The studies reviewed used several different methods of determining P_{eff} from the data from the APAP devices (P_{95}, maximal pressure during APAP titration). In most studies a single pressure was selected after a detailed review of the auto-CPAP night data. That is, periods with high mask leak were often eliminated for consideration by manual review. A single number calculated by computer from the data was not simply accepted as the proper level of pressure. Another factor to be considered in evaluating results is whether the studies were unattended or attended. In attended titration, a technologist could intervene for mask leaks that could affect the success of titration.

Two clinical series[25,47] and one randomized controlled trial[49] used unattended APAP titrations to determine a P_{eff} (optimum CPAP pressure level). An additional three clinical series[32,50,51] used attended titration and one randomized control trial used partially attended (nurse could adjust mask for significant leak) APAP titration to determine a pressure for fixed CPAP treatment.[37] Some of the investigations using attended studies quantified the number of technologist interventions.

Berkani et al.[25] used an unattended APAP titration in a regular hospital room to define P_{eff} as the maximum pressure delivered on the APAP night. Using this pressure, eight out of ten patients had an AHI < 10/hr on a fixed CPAP night using P_{eff}. Gagnadoux and coworkers[32] performed an attended APAP titration and used the P_{95} as the P_{eff} for fixed CPAP treatment. After three months of treatment a sleep study on this level of fixed CPAP found an AHI <10/hr in 21/24 patients. Lloberes used a partially attended APAP titration and compared pressures selected on the basis of APAP or manual titration using a randomized crossover design.[37] The APAP pressure (P_{95}) was 10.3±1.5 cm H_2O and the manual pressure was 10.1±1.8. In 15/20 patients the difference in pressures was 1 cm H_2O or less. Sériès et al.[47] used two weeks of unattended APAP titration to determine a P_{eff} based on the time spent below a selected reference pressure. The APAP device was set to titrate pressure between the limits P_{ref}-4 cm H_2O and P_{ref}+3 cm H_2O. The P_{ref} was selected using a formula base on BMI, AHI, and neck circumference. On fixed CPAP with P_{eff} selected by an APAP titration the AHI was <10/hr in 38/40 patients. Stradling et al.,[49] using a randomized parallel group design, found the APAP titration pressure and manual titration pressures to be very similar in two well matched groups of OSA patients (APAP: 8.2±2.1, manual CPAP titration: 8.7±2.1 cm H_2O). The selection of P_{eff} on the APAP night was performed after visualization of raw data. The pressure effective "most" of the time during APAP titration was chosen. Teschler and coworkers performed two studies in which only some of their comparisons strictly followed a randomized control design.[50,51] After an initial diagnostic night, patients were randomized to either manual or APAP titration with the alternate method to follow. The manual titration defined a P_{eff} -manual and the APAP study defined a P_{eff} taken as the P_{95}. Comparison of these pressures is consistent with a randomized controlled study. In the first study the P_{95} was on average 1.3 cm H_2O higher than P_{eff} -manual. The manual titration end point did not include elimination of snoring. Following the two titration nights, patients underwent a night of fixed CPAP on P_{95}. However, no night of fixed CPAP on a P_{eff} determined by manual titration was performed to provide a randomized comparison. The AHI on fixed CPAP using P_{eff} from APAP was 2.5±0.7/hr consistent with excellent treatment. This result suggests that P_{95} is an adequate choice for fixed CPAP. The study does not compare the outcomes of P_{95} with P_{eff} chosen by manual titration. In a second study by Teschler and coworkers,[51] a subgroup of the patients in the previously described paper were restudied at three and eight months after initial titration with both a manual CPAP titration and an APAP titration. This time the goal of the manual titration was to eliminate snoring as well as apnea and hypopnea. The results showed the P_{95} on the APAP night and manual P_{eff} to eliminate snoring to be similar. This study illustrates the point that one must consider the goals of both APAP and manual CPAP titrations when comparing their relative effectiveness.

Stradling and coworkers[49] looked at the effects of using unattended APAP titration in the sleep laboratory on subsequent acceptance of compliance with fixed CPAP treatment. They used a randomized control parallel group design, in which patients underwent either an attended conventional CPAP titration or an unattended APAP titration in the sleep laboratory, with subsequent treatment with fixed CPAP on the determined P_{eff}. The selection of P_{eff} on the APAP night was performed after visualization of raw data. The endpoint was the decision about contin-

uing CPAP treatment beyond follow-up at six weeks: acceptance, undecided, declined treatment. The percentage accepting CPAP after APAP titration was slightly but not significantly higher (73% versus 64%). However, significantly more patients with traditional CPAP titrations declined continuation of CPAP treatment (13% vs. 2% titrated with APAP, $p<0.05$). In this study no exclusion criteria were specified.

Fletcher et al.[31] studied the feasibility of using ambulatory monitoring for diagnosis followed by ambulatory APAP titration/treatment as therapy for a group with OSA. Exclusion criteria included a suspicion of other sleep disorder (narcolepsy, restless leg syndrome), complicating medical illnesses, acute decompensation requiring hospitalization, or a prior diagnosis of OSA. Of the 45 patients that underwent APAP titration, it was deemed satisfactory in 35 (78%). A satisfactory titration was defined as the ability to determine an effective treatment pressure. The criteria used to make this assessment were not specified. The investigators were able to download considerable information as the APAP device was connected to portable monitoring equipment (Horizon Surveyor). The 35 patients with satisfactory APAP titrations were offered treatment and 30 of 35 completed six weeks of APAP treatment. Those patients failing APAP titration were offered conventional titration.

In summary, four randomized control trials[37,49-51] and three clinical series[25,32,47] found that APAP could be used to select a fixed CPAP pressure that reduced the AHI to less than 10 per hour in 80%-95% of the OSA patients that were studied. Depending on the method of selection of the pressure from APAP and the manual CPAP titration protocol, the pressures from the two methods were usually within 1 or 2 cm H_2O. In nearly all studies some form of raw data was viewed before P_{eff} was selected from APAP titration (not relying solely on a machine computed number). One study[49] suggested that using APAP rather than traditional CPAP titration to define a fixed effective pressure for treatment decreased the percentage of patients declining continuation of CPAP treatment at six weeks. This question requires further study before conclusions can be reached.

Unattended APAP titration appeared able to identify an effective pressure for fixed CPAP defined as an AHI <10/hr in 38 of 40 patients in one study[47] and 8 of 10 in another.[25] In a third study, patients treated with a fixed pressure chosen by an unattended APAP titration were equally likely to accept CPAP treatment, and had an equivalent improvement in subjective sleepiness as assessed by the Epworth sleepiness scale.[49] However, in another study,[31] 22% of the patients undergoing unattended APAP titration/treatment had an unsatisfactory titration. The investigators in that study could review data from both the APAP device and a home monitoring device. Patients with "complicating medical illnesses" were excluded. More studies of larger unselected patient groups are needed to better define the efficacy of unattended APAP titration. Is the ability to view some form of raw data concerning leak, residual events and pressure over time rather than a simple summary of the amount of time at each pressure required to effectively perform unattended auto-titrations? Is monitoring of arterial oxygen saturation during unattended autotitration useful? Although not specifically addressed in the APAP studies, the availability of more extensive information should help identify patients who had an inadequate titration and to determine specific problems such as leaks. The clinician could then make a more informed decision about which patients require a subsequent traditional attended CPAP titration.

5.7 What is the evidence that auto-CPAP will increase acceptance or utilization with positive pressure treatment when used as long-term treatment for OSA?

Review of the literature identified six studies in which acceptance and/or adherence on fixed CPAP and APAP treatment were compared. Three of the six studies found that at least some aspect of adherence was improved by APAP compared to conventional CPAP. Meurice and coworkers[39] used a randomized parallel design to compare treatment with fixed CPAP and APAP. Both groups underwent determination of the optimal CPAP pressure by conventional in-laboratory titration. They were then treated with three weeks of either fixed CPAP or APAP. The same type of machine was used in either the CPAP or APAP mode. The groups were well matched with respect to AHI, the maintenance of wakefulness test (MWT) sleep latency, and the optimal CPAP pressure. There was an increase in mean nightly time at pressure over the three-week treatment period with APAP compared to fixed CPAP (6.5±1.0 versus 5.1±1.1 hours). However, the MWT mean sleep latency scores in the two groups after treatment were equivalent. Three weeks is a relatively short period of adherence monitoring. It is possible that the difference in mean nightly use may have been less with time. In any case, this study found the largest difference of any study showing an advantage for APAP with respect to adherence.

Konermann et al.[35] also used a parallel design in which patients were randomized to fixed CPAP or APAP in-lab titration followed by a three-to-six-month treatment period using the same mode of positive pressure. Adherence was determined over that period. The number of nights per week with >4 hours use was greater in the APAP group (APAP: 6.5±0.4 vs. CPAP: 5.7±0.7 night per week). The mean nightly duration of use did not differ (5.6±2.5 with CPAP vs. 5.9±1.6 with APAP), and the fixed CPAP and APAP groups were well matched. However, the exact details of the timing of when adherence monitoring occurred were not provided. Thus, one cannot determine if adherence was sampled at equivalent times in the two groups. The APAP group had more slow wave sleep on the initial treatment night. This group may have responded better on average to positive pressure and thus potentially might be more adherent. Furthermore, it was not documented that the small difference in adherence resulted in any difference in outcomes.

Hudgel and Fung[33] found an increase in the mean hours per night on APAP compared to fixed CPAP (6.0±0.3 vs. 5.5±0.3 hrs) using a randomized crossover design in a large group of patients. The Virtuoso (Respironics®), an airway vibration based device, was used for the study. The machine could be placed in either fixed CPAP or APAP mode. The level of pressure used for fixed CPAP was determined by a conventional CPAP titration. Sixty patients were randomized to CPAP or APAP as the first treatment depending on whether the last number of their hospital number was even or odd. Twenty-one did not complete the 24-week protocol because of non-compliance (19) or exclusion (2) because of medical complications unrelated to OSA. In another six patients, usage data were not available because of technical problems. Thus, 33 patients were available for analysis. A greater number had fixed CPAP before APAP (19 vs 14). The inequity in initial

treatment could have biased the results against fixed CPAP, as some patients require a period of getting acclimated to positive pressure. While the authors state that there was no evidence of a change in adherence over the three months of each treatment arm, no data on this question were presented. No statistical test of the effect of order was performed. In this study the improvement in the Epworth sleepiness scale was similar on CPAP or APAP. Thus, a small improvement in adherence may not be clinically significant. Of note, the mean pressure on APAP was lower than on CPAP by about 4 cm H_2O.

Review of the literature also revealed three studies that did not show an improvement in adherence with APAP over CPAP. In a randomized crossover study, d'Ortho and colleagues found similar adherence to CPAP and APAP.[28] Each treatment arm was three months in length and the REM plus auto device was used (Nellcor-Puritan Bennett). The authors analyzed the effect of order (APAP or CPAP first) and found this to not be significant. The authors did find that 15 of 25 preferred APAP at the end of the trial. Of note, mean nightly adherence time was short (about four hours) and the mean pressure on APAP was only about 1 cm H_2O lower than on CPAP. The relatively small pressure difference between APAP and CPAP may have been one reason a difference in adherence was not found. Teschler et al.[52] in a small study (N=10) of adherent patients also found no evidence for an increase in adherence on APAP compared to CPAP treatment. The median pressure on APAP treatment was on average about 2 cm H_2O lower than CPAP. It is possible that APAP may have less advantage in a group of patients that is very adherent to CPAP.

In a randomized control trial (crossover design), Randerath and coworkers[44] compared the mean nightly use of fixed CPAP or APAP (impedance by the forced oscillation method). The adherence (mean nightly use) did not differ between the methods of treatment (APAP: 315.4±94.7 vs. CPAP: 315±97.4 minutes). However, when the patients were asked which unit they preferred, a significantly greater number chose APAP (75% vs. 25%, $p<0.01$).

In summary, to date there is conflicting evidence about whether chronic treatment with APAP improves acceptance/adherence over fixed CPAP. It is possible that the differences in findings are secondary to different APAP devices or different patient populations. As seen from the discussion above, the mean difference between the mean APAP pressure and the fixed CPAP pressure in these studies ranges from 1 to 4 cm H_2O. It is possible that patients having a larger reduction in pressure on APAP might perceive a greater advantage to APAP. If APAP does increase adherence, whether and how the change influences clinical outcomes is as yet undefined. One of the three studies showing an advantage in adherence was relatively short in duration. It is possible that adherence may be most significantly improved over the short term. In two of the studies not showing an advantage for APAP,[43,52] the patients were very adherent on both modes of treatment. It is possible that there might be more difference in a less adherent group of patients. Even if adherence is not improved by APAP, acceptance of positive pressure treatment could theoretically be improved with these devices. This hypothesis has not been proven. A few studies found evidence of an increase in patient preference for APAP devices.[28,44] Finally, pressure intolerance is usually not the most common or important difficulty patients face with positive pressure treatment. This could limit the amount of improvement in acceptance/adherence with APAP. Treatment trials comparing APAP and CPAP also must ensure that patients randomized to different treatment arms receive equivalent support for problems such as mask leaks and dryness.

5.8 Are there safety considerations in selecting patients for auto-CPAP titration or treatment?

Safety issues are of concern, especially if APAP titration is to be performed as an unattended study. The literature search identified only two studies specifically addressing safety issues.[26,34] Boudewyns et al.[26] published a case report describing the appearance of central apneas occurring during APAP titration. The apneas occurred as pressure was increased. Some of the events seemed to occur post arousal. Of note, central apneas may also occur during manual CPAP titration. However, central apneas could conceivably result in APAP devices delivering a progressive increase in pressure. This action may not be effective in inducing a resolution of these events. If excessive pressure triggers arousals, this action could cause central apnea in some patients.[56]

Patients with lung disease and OSA, or obesity hypoventilation syndrome might also potentially have problems during unattended APAP titrations. These patients can desaturate during sleep in the absence of apnea or hypopnea, especially during REM sleep. Treatment with supplemental oxygen in addition to positive pressure or switch to bi-level pressure may be needed. This would not be available during an unattended APAP titration. Thus, it seems reasonable to expect that patients with significant heart or lung disease as well as OSA may have problems with automated titrations.

Juhasz and coworkers[34] performed an attended but automated CPAP titration in 21 patients randomly selected from a group of 162 diagnosed as having OSA. The VITPAP device they used systematically increases and then decreases pressure in steps over a set pressure range. This process allows later selection of an optimal CPAP on the basis of the AHI at each level of pressure. The device responds to arterial oxygen desaturation but not to apnea, hypopnea, or snoring. In six patients, complications developed during the titration including central apnea with arrhythmia and hypoxemia despite continued airflow (presumed hypoventilation). The patients with these complications had congestive heart failure or lung disease. In two patients, the technologist terminated the automated titration because of the development of worsening desaturation or arrhythmia. While the device used in this study is not a true APAP unit, this study does illustrate the potential problems with automated CPAP titration.

Most of the studies that were reviewed (Table 1) specifically excluded patients with heart failure or lung disease. Two trials also excluded patients on higher levels of CPAP (>14-15 cm H_2O).[35,46] It is possible that the lack of reported adverse events during APAP titration in these studies reflects judicious patient selection. Until evidence is published to the contrary, it seems prudent to exclude patients with significant lung disease, daytime hypoxemia or hypoventilation, and congestive heart failure from unattended APAP titrations. While most studies did not exclude patients needing high CPAP levels (>14 cm H_2O), the average treatment pressure in most studies was in the 8 to 12 cm H_2O range. No study specifically addressed APAP efficacy in the

group requiring high CPAP pressures. However, until further data is available, it is probably prudent to use APAP devices with the ability to provide pressures up to 20 cm H_2O for patients that might require high levels of pressure to maintain a patent upper airway (high body mass index, high AHI, large neck circumference).[61]

6.0 FUTURE RESEARCH

Review of the current literature has identified several issues that need more information. There is little or no data comparing the effectiveness of different APAP technologies. Also, the ability of APAP devices to effectively treat sleepy patients with mild OSA (AHI 5-10/hr) has not been well documented. In this review, reduction of the AHI to less than 10/hr was used to define an acceptable titration. It is acknowledged that some patients may benefit from a further reduction of the AHI to less than 5/hr. There is conflicting data about whether chronic treatment with APAP can increase acceptance of or adherence to positive pressure treatment. To date, no study has shown APAP improves patient outcomes. Perhaps specific patient subgroups might be identified in which a larger advantage can be documented for APAP.[20] For example, patients with postural or REM-related apnea could conceivably have a much lower mean nightly pressure on APAP devices. Patients exhibiting pressure intolerance during the initial titration might be another group benefiting from APAP. Studies determining whether acceptance of positive pressure treatment might be enhanced by initial treatment with APAP devices are also needed.

There is relatively little information available about the safety and efficacy of unattended APAP trials in populations with congestive heart failure, COPD, or low awake SaO_2 values. More information about patients needing high levels of CPAP is also needed. Can the built-in monitoring capabilities of the APAP devices be used to reliably tell if adequate titrations and/or treatment is occurring? Should oximetry be used during unattended auto-titration? One might expect the diagnostic capabilities of APAP devices to increase in the future. An alternative would be an interface between the APAP unit and an ambulatory monitoring device. This would allow an integrated method of diagnosis and auto-titration. More data might also help identify patients needing traditional titration or treatment with supplemental oxygen. More studies of unattended APAP titrations in CPAP naïve patients are needed to determine safety and efficacy. Does unattended APAP titration result in adequate titration in a large proportion of patients? Studies of treatment protocols using APAP titration also are needed to demonstrate that these approaches actually provide cost savings without sacrificing good patient care.

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Table 1:
Abbreviations: AHI = apnea + hypopnea index, FCPAP = fixed CPAP, APAP = autoCPAP, FOT = forced oscillation technique, FL= flow limitation, P_{eff} = optimal/ effective CPAP pressure, SN=snoring, A = apnea, H= Hypopnea, P_{95} = 95th percentile pressure (pressure exceeds this value only 5% of the time)
ESS=Epworth sleepiness scale, TST = total sleep time, MWT = maintenance of wakefulness test, RCT= randomized controlled trial

First author (year) Reference # APAP Device (what is monitored) Level of evidence	Design APAP Attended/ Unattended	N=no. of subjects Male,female Subject type: AHI Exclusions (Excl)	Protocol	Bias/comments	Outcome
Behbehani 1995 Ref:23 Prototype (snoring) Level IV	Historically controlled clinical series Attended	5 normal subjects 5 OSA subjects 4 M, 1 F in each group treated OSA pts. AHI= 49.9/hr CPAP – P_{eff}=12.6 cm H_2O Excl:none	Single study night Initial part–CPAP at fixed pressure–snoring detection studied - normals pressure = 3 cm H_2O - OSA fixed pressure chosen for comfort (3-7 cm H_2O) Second part–pressure titration	OSA patients on CPAP treatment for mean 108 days -acclimated to CPAP prior to APAP	Normals: only 3.6 pressure increases per night - device doesn't respond inappropriately to airway vibrations in normals OSA: First part of night AHI = 11.6/hr 2nd part of night AHI = 4.8/hr Conclusion: 1. APAP can effectively reduce AHI
Behbehani 1998 Ref:24 Prototype (snoring) Level II	RCT Crossover Double Blind Attended	N=31 M=26, F=5 patients already on CPAP for 8 wks AHI = 57.3±30.8 Excl: CHF	1. Diagnostic study 2. CPAP titration (P_{eff}), then treated with CPAP an average of 8 weeks 3. Randomized to 1 night of FCPAP at P_{eff} or APAP 4. Alternate treatment on the following night (Attended APAP titration)	Patients acclimated to CPAP before APAP titration Effect of order not analyzed Technician interventions on APAP not specified	FCPAP vs. APAP Equivalent improvements in AHI, sleep quality AHI CPAP = 4.2±3.8 AHI APAP = 5.4±5.4 Both APAP and CPAP significantly increased stage 3 and 4 sleep and REM and decreased sleep stage shifts. The number of sleep stage shifts was also decreased. 227.4 ±73.7 diagnostic, 180.2±53.8 CPAP, 174.5±55.3 APAP, $p<0.05$ CPAP vs. diagnostic and APAP versus diagnostic). No difference in sleep quality improvements between APAP and CPAP Lower mean pressure on APAP CPAP (P_{eff}) = 11.5±3.1 APAP mean = 8.4±3.3 APAP max = 12.8±4.3 Conclusion: 1. APAP effective 2. APAP equally effective as FCPAP 3. APAP lower mean pressure

First author (year) Reference # APAP Device (what is monitored) Level of evidence	Design APAP Attended/ Unattended	N=no. of subjects Male,female Subject type: AHI Exclusions (Excl)	Protocol	Bias/comments	Outcome
Berkani 1998 Ref: 25 REM+auto SEFAM (SN,A,H) but study using only snoring detection ability Level IV	Historically controlled clinical series Unattended	N=10 M=? F=? AHI = 55±16 Untreated patients Excl:CHF, lung Ds, cerebrovascular Dis	1. Unattended APAP titration (regular hospital room) determines P_{eff} 2. FCPAP using P_{eff} for 2 weeks 3. Ambulatory study on FCPAP P_{eff}=highest pressure administered during APAP titration –machine data only reviewed No sleep or event data for APAP titration night presented	No comparison with conventional CPAP titration Patients on CPAP for 2 wks before APAP titration	FCPAP using P_{eff} from APAP AHI = 7±5.0 cm H_2O AHI <10/hr In 8/10 Sleep quality on CPAP at P_{eff} determined by APAP: Slow-wave sleep increased from 18±26 to 73±21 min on CPAP, REM sleep increased from 36±29 min to 69±32 min on CPAP, Arousal index decreased from 47±14 to 8.3±3 events/hr on CPAP 2 patients with AHI>10: one with UPPP, one with laryngectomy had a repeat study with P_{eff}+2 cm H_2O showing an AHI <10/hr Conclusions: 1. Unattended APAP can determine P_{eff} for fixed CPAP treatment 2. snoring detection alone was adequate in most but not all patients
Boudewyns 1998 Ref: 26 Morphee Plus Vitalir (A,H) Level V	Case Report Attended	Diagnostic study: AHI=35.1/hr with 4 central apneas (CA), 168 obst. Apneas, 39 mixed apneas, 69 hypopneas	APAP titration pressure range set 5-15 mb attended titration in sleep lab	No comparison with manual titration	First REM period 9 CAs on 6-7 mbar pressure. After pressure increased above 11 mbar, a total of 60 central apneas noted (29 of them preceded by arousal) Conclusion: APAP can induce central apneas -Mechanism unknown

First author (year) Reference # APAP Device (what is monitored) Level of evidence	Design APAP Attended/ Unattended	N=no. of subjects Male,female Subject type: AHI Exclusions (Excl)	Protocol	Bias/comments	Outcome
Boudewyns 1999 Ref: 27 REM+auto SEFAM (SN, A,H) Level III	Non-RCT First APAP titration attended	N=15 M=?,F=? OSA on CPAP treatment for one year AHI=31±6 Excl: none	1. Baseline PSG 2. APAP titration attended–PSG in lab 3. Two months of APAP at home 4. APAP in lab with PSG 5. FCPAP using P_{eff} with PSG P_{eff}-determined by previous CPAP titration (on CPAP before study)	1. Patients acclimated to CPAP before APAP 2. P_{eff} determined previously-before patient entered the study 3. Order of APAP, FCPAP nights not random	APAP effective treatment, good compliance ( ) = 95% confidence interval APAP first titration AHI = 2.1 (0.9 to 3.2) APAP 2 mo: AHI = 2.5 (1.0 to 5.6) FCPAP : AHI = 1.5 (0.9 to 2.9) APAP increased the mean amount of REM sleep (26.0 to 101.5 minutes, $p<0.05$) and decreased the mean arousal index (27.4 to 8.4 events/hour, $p<0.05$) compared to baseline (no treatment). P_{eff} = 8.0(5-8) APAP mean pressure first study: 5.4 (4.5 to 6.9) APAP mean pressure 2 months: 5.4 (5.1 to 6.9) ESS baseline = 6 (4-7) after 1 month on APAP 4.0 (2 to 7) (p=NS) In 1 patient snoring /2 patients sleepiness returned on APAP Conclusions: 1. APAP effective 2. APAP as effective as FCPAP 3. APAP mean pressure lower than FCPAP

First author (year) Reference # APAP Device (what is monitored) Level of evidence	Design APAP Attended/ Unattended	N=no. of subjects Male,female Subject type: AHI Exclusions (Excl)	Protocol	Bias/comments	Outcome
D'Ortho 2000 Ref: 28 REM+auto Nellcor-Puritan Bennett (SN, A, H) Level II	RCT Crossover Single blind first APAP treatment unattended	N=25 M=22, F= 3 Untreated OSA AHI=53.3±19.0 Excl: restless legs, cardiac failure, lung disease, cerebrovascular disease	1. Ambulatory PSG for diagnosis 2. PSG in lab – CPAP titration (determines P_{eff}) 3. Randomized to 2 mo of FCPAP at P_{eff} or 2 mo of APAP 4. Home sleep study on treatment 5. Alternative treatment for 3 mo 6. Home study on treatment	Analysis showed no effect of order of treatments but no data given	APAP, FCPAP similar AHI FCPAP – 9.7±1.0 /hr APAP – 10.6±9.3 /hr Lower pressure on APAP FCPAP mean pressure = 9.7±2.6 APAP mean pressure = 8.8±1.8 cm H_2O minutes of stage 3 and 4 sleep found not to differ on CPAP (94±40) and APAP night (87±40) but to be significantly different from baseline (44±36) on both treatments. In a similar manner there was a similar decrease in awakenings and arousals per hour on CPAP (13.7±8.0/hr) and APAP 15.5±8.9 /hr) compared to baseline (45.6±25.8/hr) ($p<0.05$). ESS: Baseline (12.7±5.3), CPAP (9.2±5.5) and APAP (9.3±4.8) APAP and CPAP vs. baseline ($p<0.05$) Compliance no different FCPAP – 4.7±1.8 hrs APAP – 4.1±1.8 hrs 15/25 preferred APAP Conclusions: 1. APAP effective unattended 2. APAP as effective as CPAP 3. APAP lower mean pressure 4. APAP no increase in compliance 5. Possible increase in preference
Ficker 1998 Ref:29 REM+auto SEFAM (SN, A, H) Level II	RCT Crossover APAP attended	N= 16 M= 11 F=5 Untreated OSA AHI = 53.3±8.7 Excl:CSA, CSB, previous upper-airway surgery, cardiac disease, COPD	1. Baseline PSG 2. Conventional CPAP titration (determines P_{eff}) 3. Randomized to 1 night FCPAP using P_{eff} or APAP 4. Alternate treatment mode APAP using $P_{ref} = P_{eff}$, Pressure limits: $P_{min} = P_{ref}$ -4 mb $P_{max} = P_{ref}$ +2mb	Amount of supine sleep similar on APAP and FCPAP nights Mean APAP pressure did not differ in supine and lateral sleeping conditions? $P_{ref} = P_{eff}$ may have limited drops in APAP pressure	APAP and FCPAP had equivalent AHI FCPAP = 3.6±4.0 APAP = 4.2±5.1 Equivalent arousal index: FCPAP = 7.0±4.3 APAP = 7.4±4.1 Mean APAP pressure higher P_{eff}=7.6±2.7 APAP mean = 8.1±2.9 ESS similar after APAP (5.3±3.9) and CPAP (6.5±4.3) treatment Conclusions: 1. APAP effective 2. APAP as effective as CPAP 3. Mean APAP pressure higher

First author (year) Reference # APAP Device (what is monitored) Level of evidence	Design APAP Attended/ Unattended	N=no. of subjects Male,female Subject type: AHI Exclusions (Excl)	Protocol	Bias/comments	Outcome
Ficker 2000 Ref: 30 Somnosmart Weinman (FOT) Level II	RCT crossover double blind APAP in lab attended	N= 18 M=18, F= 0 untreated OSA AHI= 48.0 ± 28.1 Excl: upper-airway surgery, CSA,severe CHF, COPD	1. Diagnostic PSG 2. Manual pressure titration determine P_{eff} 3. Random order PSG in lab on CPAP at P_{eff} or APAP 4. PSG in lab on following night– alternate treatment	Technologist could intervene for major leaks	CPAP at P_{eff}, AHI = 4.2±3.6 APAP AHI = 3.4±3.4 AHI < 10 in 17/18 on both modes Mean Pressure (kPa) APAP = 0.84±0.26 CPAP =0.93±0.16 Largest difference in pressure in the lateral sleeping position The amounts of slow-wave (APAP: 19.3±6.6 and CPAP:18.4±7.2 %TST) and REM sleep (APAP: 21.7±4.9 and CPAP: 19.8±6.8 % TST were very similar and both significantly greater that on the diagnostic night ESS: baseline 13.3±3.0 APAP (5.6±1.8), CPAP (5.3±1.6) APAP vs. CPAP P=NS. Conclusions: 1. APAP effective 2. APAP as effective as CPAP 3. Lower mean pressure on APAP in most but not all patients 4. Equivalent improvements in sleepiness (ESS) on APAP and CPAP
Fletcher 2000 Ref:31 Horizon DeVilbiss (SN, A, H) Level IV	Historically controlled clinical series initial APAP titration and subsequent APAP treatment unattended	N=45 M=?, F=? Untreated OSA Excl: suspicion of other sleep disorder (narcolepsy, restless leg syndrome), complicating medical illnesses, acute decompensation	1. Ambulatory diagnostic study 2. Ambulatory APAP titration (2 nights if needed) (Unattended) Data visually reviewed in detail 3. Offered APAP treatment at home if titration satisfactory DeVilbiss-Surveyor used to obtain ambulatory data	Detailed review of machine data performed to assess quality of titration Protocol used to assess adequacy of titration not specified	Feasibility of Unattended APAP titration/ treatment 45 offered APAP titration 35 titration adequate, offered treatment 30 completed 6 wks of APAP treatment N=30 Baseline AHI = 34.1±4.0 APAP AHI = 8.6±0.8 N=30 ESS baseline=16.8±0.6, after treatment 10.5±0.9, p<0.01) N=26 had compliance tested at 3 wks 4.0±2.1 hours N=26, MSLT after treatment the nap sleep latency was significantly greater that at baseline (5.7±0.81 vs. 3.7±0.6, p<0.01). Conclusions: 1. Unattended APAP-satisfactory titration in many patients (35/45) 2. APAP effective treatment

First author (year) Reference # APAP Device (what is monitored) Level of evidence	Design APAP Attended/ Unattended	N=no. of subjects Male,female Subject type: AHI Exclusions (Excl)	Protocol	Bias/comments	Outcome
Gagnadoux 1999 Ref 32 Autoset-ResMed (SN,A,H, FL) Level IV	Historically controlled clinical series Attended APAP titration in lab	N =24 M=?, F=? Untreated OSA AHI 69.6±29.8 Excl: none	1. Baseline PSG 2. APAP defines P_{eff} as the P_{95} pressure 3. FCPAP at P_{95} for 3 mo 4. Ambulatory PSG on FCPAP at P_{95}	Technician could adjust mask (0.93±0.46 times per night) No comparison with CPAP on P_{eff} determined by conventional titration	Attended APAP AHI = 5.7±4.8 21/24 patients AHI <10/hr Adequacy of APAP to determine P_{eff}: Home study shows AHI at 3 months FCPAP = 5.25±1.82 with 21/24 have AHI < 10/hr On CPAP at a pressure selected by APAP: slow wave increased (from 17.4 to 39.5% TST, p<0.001) and REM sleep increased (from 9 to 18.8 %TST, p<0.001) compared to the diagnostic night ESS significantly decreased after treatment(11.4±5.4 to 5±4, p<0.05) Conclusions: 1. APAP effective 2. APAP as effective as CPAP(P_{95}) 3. P_{95} of APAP titration can choose P_{eff} for fixed CPAP
Hudgel 2000 Ref 33 Virtuoso Respironics (SN) Level II	RCT Crossover APAP treatment unattended	N=60 M=?,F=? Untreated OSA, UARS N=39 completed study N=33 compliance data available N=33 AHI =27±4 Excl: COPD, CHF, upper airway surgery	1. Diagnostic or split night 2. CPAP titration if needed defines P_{eff} 3. Randomized to FCPAP or APAP for 6 weeks 4. Crossover to alternate treatment for 6 weeks ESS, compliance assessed at 6 weeks 35 randomized to CPAP first 25 randomized to APAP first	N=33 completed study with compliance data: 19 FCPAP first 15 APAP first possible order effect possible not analzyed	Home treatment with FCPAP vs APAP Mean nightly pressure lower on APAP FCPAP = 10.6±0.4 cm H_2O APAP = 6.4±0.4 (p< 0.001) Mean nightly use higher with APAP (N=33) (6.0±0.3 vs. 5.5±0.3 hrs) (P=0.04) ESS not different between FCPAP/APAP FCPAP = 8±1 APAP= 9±1 both significantly lower than baseline (16±0.8) Conclusions: 1. Mean nightly pressure lower on APAP 2. Mean nightly use higher on APAP 3. Equivalent improvement in ESS on APAP and CPAP
Juhasz 1996 Ref: 34 VITPAP Vitalong Level IV	Historically controlled clinical series Attended titration	N=21 M=?, F=? Untreated OSA AHI = 52.1±29.1 Excl: none	1. Baseline study 2. Unattended CPAP titration with VITPAP, monitoring with Vitalog 3. Conventional CPAP titration-partial PSG	VITPAP–sequentially raises pressure to allow selection of P_{eff} Responds only to drops in SaO_2 Not a true APAP device	15/21 patients no problems 5/21 central apneas 5 developed hypoventilation on CPAP 6 patients required technician intervention to lower pressure or terminate study

First author (year) Reference # APAP Device (what is monitored) Level of evidence	Design APAP Attended/ Unattended	N=no. of subjects Male,female Subject type: AHI Exclusions (Excl)	Protocol	Bias/comments	Outcome
Konermann 1998 Ref: 35 Horizon DeVilbiss (SN, A, H) Level I	RCT Parallel Single blind First APAP in lab attended	N =50 M=44, F= 6 untreated OSA group receiving FCPAP baseline AHI = 38.3±13.9 APAP baseline AHI= 35.5±9.6 Excl: If CPAP > 14 cm H_2O	1. Baseline PSG 2. Randomized to FCPAP or APAP 3. In lab titration FCPAP or APAP 4. 3-6 months later had PSG, portable PSG as well, machine compliance checked	Groups appear equivalent Method of determining compliance–number of nights sampled etc in each group not well detailed	APAP, FCPAP equal AHI FCPAP = 4.4±3.6 APAP = 2.4±1.7 More slow-wave sleep on APAP: slow wave sleep increased from 11.4±10.4%TST on a diagnostic night to 17.6±18.4 on CPAP versus 13.2±12.2 on a diagnostic night to 27.2±16.5 on APAP ($p<0.01$ APAP vs CPAP) Compliance better on APAP (nights per week with use >4 hrs) 6.5±0.4 vs. 5.7±0.7, $p<0.01$ However, no difference in mean hours per night 5.9±1.6 versus 5.6±2.5 Conclusions: 1. APAP effective 2. APAP as effective as FCPAP 3. Some measures of compliance better with APAP
Lafond 1998 Ref: 36 Horizon DeVilbiss (SN, A, H) Morphee-plus, Pierre Medical (A,H) Level II	RCT one machine vs. the other Attended	N = 8 M = 8 only 7 studies with both machines treated OSA patients using nasal CPAP at home AHI = 53 /hr exclusions: not specified	1. Two study nights 2. Randomly assigned to each device 3 Alternate device on next night Nasal resistance increased acutely by histamine Response of mask pressure noted	Two subjects had both machines on one night	After increased in nasal resistance: Morphee plus–mask pressure decreased Horizon–mask pressure did not increase except in 1 patient Conclusion: 1. Neither device responsed appropriately

First author (year) Reference # APAP Device (what is monitored) Level of evidence	Design APAP Attended/ Unattended	N=no. of subjects Male,female Subject type: AHI Exclusions (Excl)	Protocol	Bias/comments	Outcome
Lloberes 1996 Ref:37 Autoset T ResMed (SN,A,H,FL) Level II Level IV	RCT Crossover For main part of study N=20 Historically controlled clinical series N = 9 APAP titration "partially" attended (nurse could correct mask placement if leaks detected)	N =20 M=?, F=? Untreated OSA AHI = 53.3±19.0 Excl: not specified	1. Baseline PSG 2. Randomized to manual CPAP titration with PSG or partially attended APAP titration 3. Alternate titration "visual" P_{eff} selected from APAP night = highest pressure after Visual review eliminated periods of high leaks Additional study: N=9 had full PSG during APAP titration	APAP choice of P_{eff} required visual review of raw data ("APAP visual') Effect of order not analyzed Using automatic machine calculation of P_{95} resulted in higher P_{eff} P_{eff} from manual titration night = highest pressure in REM sleep in the supine position	N=20, APAP, FCPAP equivalent optimal pressure- P_{eff} APAP "visual" P_{eff}=10.3±1.5 CPAP P_{eff} =10.1±1.8 15/20 difference in pressures was 1 cm H_2O or less Machine computed 95th percentile pressure = 11.5±2.9 (included periods of high leaks?) N=9 PSG on APAP AHI = 5.6±6 Arousal index = 12±7/hr conventional CPAP titration: arousal index 11±6 /hr Conclusions: 1. APAP is effective in reducing AHI 2. APAP can be used to select P_{eff}–gives similar P_{eff} as manual titration 3. Machine computed P_{95} may be higher than a visually determined pressure where periods of leaks are eliminated
Lofaso 1996 ref: 38 REM+ with MC – SEFAM (Sn, A, H) In this study only SN used Level IV	Historically controlled clinical series APAP Attended	N=15 M= 15 F=0 58±9 yrs Untreated OSA AHI=51±31 Excl: CHF, lung Ds., RLS, CVD	1. Diagnostic study (airflow by nasal-oral thermistor) 2. APAP night with PSG Apnea/hypopnea detection of APAP device disabled for this study	1. No comparison with FCPAP 2. Could technician intervene for mask leaks? 3. REM sleep was not improved implying less than perfect effectiveness	APAP AHI = 12±21 /hr 12/15 patients did have AHI < 10/hr 3/15 had AHI > 10/hr one without snoring, two mouth breathers On APAP slow-wave sleep increased (102±149 minutes vs. 71±86 on the diagnostic study Conclusion: 1. APAP with snoring alone effective in reducing AHI in most but not all OSA patients
Meurice 1996 Ref:39 Morphee-plus, Pierre Medical (A,H) Level II	RCT Parallel APAP treatment at home unattended APAP in lab not clearly specified ? attended	N=16 M=16, F=0 untreated OSA AHI =43.6±19.8 Excl: not specified	1. Baseline PSG 2. Manual CPAP titration determines P_{eff} 3. Randomized to 3 wks of home treatment with FCPAP using P_{eff} or APAP 4. In lab PSG on treatment mode 5. MWT determined before and after APAP Pressure range: (P_{eff} -4 cm H_2O, P_{eff} +2cm H_2O)	1. Groups given FCPAP and APAP equivalent in AHI, MWT 2. Settings of APAP depended on P_{eff}	FCPAP, APAP same AHI, sleep quality Study on treatment FCPAP AHI = 9.0±3.0 APAP AHI = 10.1±2.5 Mean nightly (time at pressure) use better with APAP (6.5±1.0 vs. 5.1±1.1 hrs) ESS and MWT sleep latency after Rx improved on both APAP and CPAP–no difference between APAP and CPAP in the improvement Conclusions: 1. APAP effective 2. APAP as effective as FCPAP 3. Better compliance with APAP 4. MWT sleep latency not different between treatments

First author (year) Reference # APAP Device (what is monitored) Level of evidence	Design APAP Attended/ Unattended	N=no. of subjects Male,female Subject type: AHI Exclusions (Excl)	Protocol	Bias/comments	Outcome
Miyazaki 1999 Ref: 40 Virtuoso, Respironics (SN) Level II	RCT APAP attended	N=11 M=10, F=1 OSA ? treated or untreated AHI = 68.3±20.2 Excl: not specified	Attended FCPAP titration, APAP alternated every hour	Not controlled for sleep stage Maximum not mean pressure compared	AHI supine (/hr) baseline = 68.3±20.2 CPAP = 0.5±0.9 APAP = 9.6±14.5 (p=NS) Max. Pesophagus CPAP = - 11.9±7.2 APAP= -26.0±13.7 Conclusions: 1. AHI improved on both but CPAP more improvement although p=NS 2. Maximum esophageal pressure deflections higher with APAP
Randerath 1999 Ref: 41 Somnosmart (Weinmann, Hamburg, Germany) using forced oscillation technique (FOT) Level II modes of FOT Level IV effectiveness of APAP	Historically controlled clinical series Effectiveness of APAP-FOT RCT Crossover 2 modes of APAP-FOT APAP titration Attended	N=11 M=11, F=0 Untreated OSA patients AHI 31.6±26.6 Excl: none	1. Diagnostic PSG 2. Manual CPAP titration- P_{eff} determined by MD review 3. APAP-FOT in mode 1 or 2 (random) 4. APAP-FOT in alternate mode Two modes of APAP compared: mode #1 pressure limits 4 to 15.5 mode #2 max. pressure = P_{eff} + (15.5-P_{eff})/2	No comparison with manual titration CPAP efficacy	Baseline AHI: 31.6±26.6 Mode 1 APAP AHI: 3.4±4.1 Mode 2: APAP AHI 5.0±7.2 Pressures: manual P_{eff}=9.3±2.1 Mean pressure APAP mode 1=5.4±1.0 Mean pressure APAP mode 2=5.1±0.7 increase in REM sleep (from 42.7±16.4 min on the diagnostic night to 66.6±23.4 APAP mode 1 and 61.1±24.6 APAP mode 2) decrease in the respiratory arousals/hour (20.9±16.6-diagnostic to 2.3±3.7/hr - APAP mode 1, and 4.5±5.2 mode 2, p<0.001). Conclusions: 1. APAP-FOT effective 2. APAP-FOT–requires lower mean pressure than P_{eff} 3. The 2 APAP modes studied were equivalent in lowering AHI and improving sleep quality
Randerath 2000 Ref: 42 same as above using FOT Level II modes of FOT Level IV effectiveness of APAP	Historically controlled clinical series Effectivenss of APAP-FOT RCT Crossover 2 modes of APAP-FOT APAP attended	N= 10 M= 9, F=1 Untreated OSA AHI= 18.3±13.3 Excl: none	1. Diagnostic PSG 2. Manual CPAP titration- P_{eff} determined by MD 3. APAP-FOT in mode 1 or 2 (random) 4. APAP-FOT in alternate mode Mode #1 pressure limits 4 to 15.5 mode #2 minimum pressure = P_{eff} - (P_{eff} - 4)/2	No comparison with manual titration CPAP efficacy Mild group of OSA	AHI: baseline = 18.3±13.3, Mode 1 APAP AHI = 2.5±1.9, Mode 2 APAP AHI = 1.8±0.7. Manual CPAP P_{eff}=8.0±1.3 Mean pressure mode 1=5.6±2.1 Mean pressure mode 2=7.3±1.6 Conclusions: 1. APAP-FOT effective 2. APAP-FOT–requires lower mean pressure than P_{eff} 3. The 2 APAP modes studied were equivalent in lowering AHI and improving sleep quality

First author (year) Reference # APAP Device (what is monitored) Level of evidence	Design APAP Attended/ Unattended	N=no. of subjects Male,female Subject type: AHI Exclusions (Excl)	Protocol	Bias/comments	Outcome
Randerath 2001 Ref: 43 Somnosmart Weinmann (FOT) Level I	RCT Crossover single blind Partially attended No technologist interventions on APAP	N=52 M=45, F=7 Untreated OSA AHI = 32.1±5.8 Excl: not listed	1. Diagnostic PSG 2. CPAP titration determines P_{eff} 3. CPAP in lab (1st week) 4. APAP in lab 5. Randomized to 6 wks with APAP or CPAP 6. Study in lab on treatment 7. Alternate treatment for 6 weeks. 8. study in lab on alternate treatment 9. Preference assessed	CPAP first night preceded APAP first night Not specified if technologist could intervene for mask leaks	APAP first wk , AHI=5.3±5.6 CPAP first wk, AHI=4.6±4.8 APAP 6wks, AHI=5.0±5.2 CPAP 6 wks, AHI=4.3±6.3 REM sleep increased from 47.4±25.3 to 63.4±27.2, p<0.05 and the respiratory arousal index decreased 17.8±15.8 to 3.3±3.9/hr, p<0.001) on APAP compared to the diagnostic night Mean pressure lower on APAP APAP 5.7±1.8 cm H_2O vs. CPAP 7.8±1.5, p<0.001 Compliance: use per night APAP 315.4±94.7 minutes CPAP 315.4±97.4 minutes, ns Preference: APAP (75%), CPAP (25%), p<0.01 Conclusions: 1. APAP effective 2. APAP as effective as CPAP 3. Lower mean pressure on APAP 4. Equal compliance 5. More preferred APAP
Randerath 2001 Ref: 44 Somnosmart Weinmann (FOT) Level II	RCT Crossover single blind APAP in lab attended ?	N=25 M=20, F=5 Untreated OSA AHI = 32.1± 18.1 Excl: UPPP, COPD, Neuro/ Psychiatric Disease	1. Diagnostic PSG 2. Manual pressure titration 3. Random order PSG in lab on CPAP at P_{eff} or APAP 4. PSG in lab on alternate treatment	Subjects not really blind to mode Manual CPAP titration based on thermistor	AHI APAP=5.5±3.8 AHI CPAP=6.6±8.7 Mean pressure: APAP=5.5±2.1 mbar CPAP=8.3±1.6 mbar (p<0.001) Sleep quality questionnaire: sleep quality better on APAP Conclusions: 1. APAP effective 2. APAP as effective as CPAP 3. Lower mean pressure on APAP 4. Sleep quality subjectively better on APAP

First author (year) Reference # APAP Device (what is monitored) Level of evidence	Design APAP Attended/ Unattended	N=no. of subjects Male,female Subject type: AHI Exclusions (Excl)	Protocol	Bias/comments	Outcome
Scharf 1996 Ref: 45 Horizon Autoadjust DeVilbiss (SN, A, H) Level II	RCT Crossover Single blind APAP attended	N=12 M=8, F=4 Untreated OSA AHI = 57.3± 30.8 Excl: asthma, COPD, CHF, allergic rhinitis	1. Diagnostic PSG 2. CPAP titration- determines P_{eff} 3. FCPAP at home 2 wks. 4. Randomized to FCPAP or APAP each with PSG for one night (same machine-different modes) 5. Alternate treatment for one night	Patients already on 2 weeks of CPAP before APAP titration No analysis of effect of order of study nights APAP titration–attended	AHI FCPAP = 3.8±2.5 AHI APAP = 4.4.±2.2 On APAP - 63% of night at pressure below P_{eff} 16.1±22.7 minutes of slow-wave sleep on conventional CPAP and 32.6±27.4 minutes on APAP, $p<0.05$ APAP vs. CPAP Conclusions: 1. APAP effective 2. APAP as effective as CPAP 3. More slow-wave sleep on APAP 4. APAP lower mean pressure
Series 1997 Ref: 46 MorpheePlus Pierre-Medical (A, H) Level II	RCT Parallel Single blind APAP treatment unattended APAP for control study-attended?	N=36 M=?, F=? Untreated OSA AHI=43.6±19.8 Excl: periodic breathing, life threatening hypersomnia, narcolepsy, PLMs, estimated pressure above 15 cm H_2O	1. Diagnostic (baseline) study 2. Manual titration – defines P_{eff} 3. Randomized to one of 3 goups with treatment for 3 weeks group 1 = FCPAP on P_{eff} group 2 = APAP with $P_{ref} = P_{eff}$ group 3 = APAP with $P_{ref} = P_{est}$ 4. PSG at 3 weeks on treatment mode used at home ("control study") APAP pressure limits (P_{ref} +3, P_{ref} -4 cm H_2O) P_{est} computed from formula Depending on AHI, BMI, neck circumference	3 groups equivalent in BMI but AHI higher in group 3 P_{est} calculation similar in all 3 groups	Change in AHI from baseline to control study was the same in all groups Increase in slow wave and REM sleep and decrease in the arousal index similar in all 3 groups Change in ESS (improvement)similar in all 3 groups after treatment Group 1: -8.2 ± 5.3 Group 2: -6.5 ± 4.2 Group 3: - 9.1 ± 4.9 Similar improvements in the MWT were noted in all 3 groups Pressure time index-% of machine on time at which pressure applied was higher in FCPAP group Time counter the same in all 3 grps. Patients with CPAP>4hrs for 5d/wk or more Group 1 = 9/12, Group 2 =11/12, Group 3 = 12/12 Conclusions: 1. APAP effective 2. APAP as effective as FCPAP 3. Compliance similar 4. APAP with P_{est} is effective

First author (year) Reference # APAP Device (what is monitored) Level of evidence	Design APAP Attended/ Unattended	N=no. of subjects Male,female Subject type: AHI Exclusions (Excl)	Protocol	Bias/comments	Outcome
Series 2000 Ref: 47 MorpheePlus Pierre-Medical (A, H) Level I for 1 vs 2 weeks Level IV for effectiveness	Historically controlled clinical series Unattended APAP titration	N=42 M= ?, F=? Consecutive untreated OSA AHI = 43.6±19.8 Excl: none	1. Diagnostic study 2. Home APAP titration for 1 or 2 weeks (random) 3. Pressure information downloaded and P_{eff} determined 4. 6 wks home treatment on FCPAP at P_{eff} 5. Lab sleep study on P_{eff}	APAP pressure limits (cm H_2O): $P_{min} = P_{ref} - 4$ $P_{max} = P_{ref} + 3$ P_{ref} computed from formula based on AHI,BMI, neck circumference P_{eff} determined based on % of time pressure below P_{ref}	No difference between 1 and 2 weeks of home titration On FCPAP at P_{eff} determined by APAP AHI=4.8±6.0 , AHI<10/hr in 38/40 ESS reduced on FCPAP at P_{eff} chosen by APAP from a baseline of 15±4 to 7±3, $p<0.05$ Conclusions: 1. Unattended APAP titration effective at choosing P_{eff} for chronic FCPAP treatment. 2. No difference between 1 or 2 weeks of home APAP titration
Sharma 1996 Ref: 48 prototype-sensing snoring Respironics Level II	RCT Crossover Double blind Attended APAP titration	N=20 M=19, F=1 Untreated OSA AHI=50.8±28.8 Excl: Upper-airway surgery in last 6 mo, lung ds, cardiac ds., CNS disease	1. Diagnostic night 2. Randomized to manual or APAP titration 3. Alternate titration	Technician could intervene on APAP titration nights 5 patients required technician intervention for pressure adjustment on APAP lower minimal SaO_2 on APAP	CPAP and APAP AHI similar Manual titration: AHI = 3.8±3.1 APAP: AHI = 6.3±5.3 Lower pressure on APAP 10.1±3.8 vs. 12.3±3.9 Slow-wave sleep (as % of TST) did not differ on CPAP (16.7±9.8) and APAP (17.1±9.3) nights. REM sleep (% TST) on CPAP (22.7±7.9) and APAP (25.3±7.4) nights did not differ. Conclusions: 1. APAP effective 2. APAP as effective as CPAP 3. Pressure was lower on APAP
Stradling 1997 Ref: 49 Horizon DeVilbiss (SN, A, H) Level I	RCT Parallel Unattended (personal communication from J Stradling)	N =112 M=?, F=? AHI note reported Excl: none	1. Diagnostic study 2. CPAP titration– randomly assigned to conventional technician titration or APAP titration–used to determine P_{eff} 3. Chronic treatment with fixed CPAP using DeVilbiss Revitalizer for 6 wks. 4. Acceptance determined P_{eff} determined the next day by review of raw data for both types of titration	1. Groups randomized to each titration arm were equivalent 2. Raw data examination required to select P_{eff} on APAP	P_{eff} manual = 8.7±2.1, P_{eff} APAP = 8.2±2.1 Acceptance of CPAP at 6 weeks: Equivalent rates of success on CPAP With manual (64%) and APAP titration (73%) Equivalent ESS at 6 wks in both groups of those complying More failure to accept CPAP with conventional titration (13% vs. 2%) Conclusion: 1. APAP titration results in similar if not better acceptance of CPAP than manual titration.

First author (year) Reference # APAP Device (what is monitored) Level of evidence	Design APAP Attended/ Unattended	N=no. of subjects Male,female Subject type: AHI Exclusions (Excl)	Protocol	Bias/comments	Outcome
Teschler 1996 ref: 50 Autoset-ResMed (SN,A, H,FL) Level IV N1 vs N4 Level II N2 vs N3	Historically controlled clinical series N1 vs N4 RCT Crossover N2 vs N3 Attended APAP titration	N=20 M=20, F=0 Untreated OSA AHI:60.3±5.7 Excl: Resp. failure, upper airway infection, PLMs, nasal deformity	1. Diagnostic PSG (N1) 2. Randomized to manual CPAP titration (P_{eff} determined) or APAP titration (P_{95} determined) by an attended in lab PSG (N2) 3. Alternate method of titration (N3) 4. PSG on fixed pressure determined by APAP– P_{95} (N4) P_{95}=95% percentile pressure excluding periods of high leaks, determination blind to results of manual CPAP titration APAP – attended titration, tech could intervene for leaks	Manual titration did not attempt to eliminate snoring or flow limitation PSG on fixed pressure at P_{eff} (manual titration) NOT compared with PSG on fixed pressure at P_{95}	AHI manual titration = 10.1±3 AHI APAP titration: = 2.8±0.9 AHI FCPAP at P_{95} = 2.5±0.7 P_{95} on APAP was on average 1.3 cm H_2O higher than P_{eff} chosen by manual titration (N2 vs. N3) Conclusions: 1. APAP effective 2. APAP as effective as FCPAP 3. P_{95} on Autoset gives good P_{eff} for FCPAP
Teschler 1997 ref:51 Autoset-ResMed (SN,A, H,FL) Level IV Efficacy of P_{95} Level II P_{eff} vs P_{95}	RCT Crossover (comparing P_{eff} and P_{95}) DB-investigator chosing P_{95} blind to P_{eff} on manual CPAP titration Historically controlled clinical series Efficacy of P_{95} as FCPAP, Constancy of P_{95} Attended APAP titration	N=20 M=20, F=0 untreated OSA AHI=60.3±5.7 Excl: CHF, TIA, respiratory failure, nasal pathology	1. Diagnostic PSG 2. Random order 3 & 4 3. Manual CPAP titration -determines P_{eff} -no attempt to eliminate snoring, FL 4. Attended APAP titration determines P_{95} 5. PSG on FCPAP with P_{eff} =P_{95} P_{95}=95 percentile pressure after excluding periods of high leaks 6. Home treatment with FCPAP at P_{95} for 3 months 7. Home studies on FCPAP 8. Lab PSG–repeat manual CPAP and APAP titrations (3 mo study) with manual titration to eliminate SN and FL 9. Home treatment with FCPAP at new P_{95} for another 5 mo 10. Eight month studies as at 3 months	Initial part of study same subjects and data as Teschler 1996 CPAP titration criteria between initial study (n=20) and 3 and,8 month study (n=16) were different Mean body weight constant over 8 months Presumably manual and APAP titrations with full PSG at 3 and 8 months were in random order as in the initial study but this was not clearly stated.	In lab titrations: AHI APAP = 2.8±0.9 AHI manual titration night = 10.1±3.1 (snoring not eliminated) AHI FCPAP on P_{95} pressure = 2.0±0.9 Initial in lab study (n=20): Autoset P_{95} higher than manual P_{eff} APAP (P_{95})=9.9±0.4 cm H_2O P_{eff} (manual titration) =8.6±0.4 (p=0.001) N=16 study: P_{eff} (manual titration using new criteria) and P_{95} (home APAP titrations) were similar As expected P_{eff} manual titration higher with new criteria: 3 mo: P_{eff} =11.0±0.5, P_{95} = 10.6±0.4 8 mo: P_{eff} =10.4±0.4, P_{95} = 9.7±0.5 P_{95} constant by APAP over 8-month period Conclusions: 1. APAP effective in reducing AHI 2. APAP as effective in reducing AHI as CPAP 3. APAP P_{95} higher than P_{eff} on manual titration if the goal of manual titration is not to eliminate snoring

First author (year) Reference # APAP Device (what is monitored) Level of evidence	Design APAP Attended/ Unattended	N=no. of subjects Male,female Subject type: AHI Exclusions (Excl)	Protocol	Bias/comments	Outcome
Teschler 2000 ref: 52 Autoset-ResMed (SN,A, H,FL) Level II	RCT Crossover DB APAP in lab Attended? (not clearly stated)	N=10 M=10, F= 0 Untreated OSA AHI = 52.9 ± 8.1 Excl; asthma, COPD, CHF, allergic rhinitis	1. Diagnostic night 2. Manual CPAP titration-determined P_{eff} 3. Randomized to FCPAP on P_{eff} or APAP for 2 months 4. Home studies (12) over 2 mo. 5. Alternate mode of treatment 6. Home studies (12) over 2 mo. 7. Lab PSG 0,60, 120 days on APAP (study constancy of required pressure) P_{eff} goal-elminate apnea, hypopnea, snoring but not flow limitation unless associated with hypopnea	Manual titration-no attempt to eliminate flow limitation unless with hypopnea Same group studied in 1996 paper with additional follow-up	APAP, FCPAP equally effective Rx AHI (machine scored) – FCPAP = 0.58±0.1 APAP = 0.53±0.1 Lower median pressure on APAP P_{eff} = 9.4±0.6 P_{median} on APAP = 7.6±0.4 (lab) P_{median} on APAP = 7.2±0.4 (home) On APAP slow-wave sleep increased (from 10.2±2.2 to 24.6±2.8 as a % of TST, $p<0.01$) and REM sleep increased (from 11.7±2.3 to 25.9±1.4 %TST, $p<0.001$) on compared to the diagnostic night On APAP the respiratory arousal index decreased from 42±7.2 /hr to 4.8±0.8 /hr, $p<0.001$) Equal mean nightly use (both >6 hrs) FCPAP avg use = 6.1±0.5 hrs. APAP pavg use = 6.3±0.4 No change in APAP-recommended titration pressures over 2 months P_{95} APAP pressures on home studies and lab studies greater than P_{eff} Conclusions: 1. APAP effective 2. APAP as effective as CPAP 3. Median Pressure lower on APAP 4. APAP P_{95} higher than P_{eff} 5. APAP and FCPAP compliance similar